

IN THE SPECIFICATION

Replace current pages 4, 5 and 7 with the attached replacement pages.

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system of modular construction, in particular for extra-corporal detoxification, enabling a reduction of the plasma and tissue levels specific to the patient.

Inter alia, the invention is based on the knowledge that $\text{TNF}\alpha$ has a key role to play in this regulation system. It is released inter alia by macrophages as a result of various "external" influences such as injuries, inflammations, infections, septicaemia and induces a local and systemic activation of the unspecific and specific defence system via a cytokine cascade (IL-1, IL-6). Clinically, a massive $\text{TNF}\alpha$ release is expressed by increased body temperature, lack of appetite and all the subsequent symptoms of a catabolic metabolism situation. In pathogenesis of the sepsis, activation of the macrophages and thus the release of $\text{TNF}\alpha$ appears to be of essential importance for the survival of the patient in the early phase of this disease, whereas the continued state of activation results in the de-compensation of all defence reactions in the further course.

The task of the invention was solved by an immunoadsorber for use in sepsis therapy. The immunoadsorber according to the invention is particularly used for the removal of complement factors and lipopolysaccharides (LPS) as well as the removal of further sepsis mediators, and also TNF and interleukins from body fluids, if need be. It is characterised by carrier materials of organic or synthetic polymers, to which both poly or monoclonal antibodies aimed against the complement factors C3a and/or C5a, and also antibodies aimed against lipopolysaccharides (LPS) are bound. In a preferred embodiment, antibodies aimed against further sepsis mediators are also bound to the carrier.

Preferably, these are polyclonal antibodies, particularly preferably avian antibodies of type IgY. The antibodies against sepsis mediators are contained according to the state of the dysregulation.

According to this invention, these are antibodies aimed against TNF, IL1, IL6, IL8 and/or IL10.

Preferred antibodies against the complement factor C3a manifest specific activity against at least one of the following peptide sequences:

NH_2 -KCCEDGMRQNPMR-COOH (SEQ ID NO: 1)

NH_2 -RFSCQRRTRFISL-COOH (SEQ ID NO: 2)

NH_2 -ITELRRQHARAS-COOH (SEQ ID NO: 3)

Preferred antibodies against the complement factor C5a possess specific activity

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against at least one of the following peptide sequences:

NH₂-QADYKDDDDKLPAE-COOH (SEQ ID NO: 4)

NH₂-DDKLPAEGLDIENS-COOH (SEQ ID NO: 5)

Preferred antibodies against IL1 α/β possess specific activity against at least one of the following peptide sequences:

NH₂-NCYSENEEDSSSID-COOH (SEQ ID NO: 6)

NH₂-GAYKSSKDDAKIT-COOH (SEQ ID NO: 7)

NH₂-WETHGTKNYFTS-COOH (SEQ ID NO: 8)

NH₂-RISDHHYSKGFRQA-COOH (SEQ ID NO: 9)

NH₂-VQGEESNDKIPVA-COOH (SEQ ID NO: 10)

NH₂-ESVDPKNYPKKKMEKRF-COOH (SEQ ID NO: 11)

Preferred antibodies against IL6 possess specific activity against at least one of the following peptide sequences:

NH₂-APHRQPLTSSERIDKQI-COOH (SEQ ID NO: 12)

NH₂-QNRFESSEEQARA-COOH (SEQ ID NO: 13)

NH₂-AITTPDPTTNAS-COOH (SEQ ID NO: 14)

Preferred antibodies against IL10 possess specific activity against at least one of the following peptide sequences:

NH₂-SPGQGTQSENSCT-COOH (SEQ ID NO: 15)

NH₂-QMKDQLDNLLKES-COOH (SEQ ID NO: 16)

NH₂-MPQAENQDPDIKA-COOH (SEQ ID NO: 17)

NH₂-LPCENKSKAVEQ-COOH (SEQ ID NO: 18)

Preferred antibodies against TNF α possess specific activity against at least one of the following peptide sequences:

NH₂-VRSSSRTPSDKPVA-COOH (SEQ ID NO: 19)

NH₂-KSPCQRETPEGAEAKPW-COOH (SEQ ID NO: 20)

The immunoadsorber according to the invention manifests membranes or particles customary per se of organic or synthetic polymers as carrier materials, e.g. of polystyrenes, carbohydrates such as cellulose or agarose derivatives, or of acrylates, with the specific antibodies being covalently linked to them or fixed to them via

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The invention is explained in more detail by the following examples:

Example 1

Production of polyclonal antibodies by means of immunogenic peptides:

The peptides listed in Table I are produced by means of a solid phase synthesis: Table I

| Peptide sequence | Antigen |
|-----------------------------------|---------------|
| KCCEDGMRQNPMR (SEQ ID NO: 1) | C3a |
| RFSCQRRTRFISL (SEQ ID NO: 2) | |
| ITELRRQHARAS (SEQ ID NO: 3) | |
| QADYKDDDDKLPAE (SEQ ID NO: 4) | C5a |
| DDKLPAEGLDIENS (SEQ ID NO: 5) | |
| SPGQGTQSENSCT (SEQ ID NO: 15) | |
| QMKDQLDNLLLKES (SEQ ID NO: 16) | IL10 |
| MPQAENQDPDIKA (SEQ ID NO: 17) | |
| LPCENKSKAVEQ (SEQ ID NO: 18) | |
| NCYSENEEDSSSID (SEQ ID NO: 6) | IL 1 α |
| GAYKSSKDDAKIT (SEQ ID NO: 7) | |
| WETHGTKNYFTS (SEQ ID NO: 8) | |
| RISDHHYSGFRQA (SEQ ID NO: 9) | IL1 β |
| VQGEESNDKIPVA (SEQ ID NO: 10) | |
| ESVDPKNYPKKKMEKRF (SEQ ID NO: 11) | |
| APHRQPLTSSERIDKQI (SEQ ID NO: 12) | IL6 |
| QNRFESSEEQARA (SEQ ID NO: 13) | |
| AITTPDPTTNAS (SEQ ID NO: 14) | |
| VRSSSRTPSDKPVA (SEQ ID NO: 19) | TNF α |
| KSPCQRETPEGAEAKPW (SEQ ID NO: 20) | |

These peptides are covalently bound to a carrier (KLH) according to a standard recipe. The conjugate dissolved in PBS is mixed in equal shares with Freund's adjuvant. The individual inoculation dose is set in such a way that it contains 200pg of the peptide belonging to the antigen in question. 15-week-old young hens are im-

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(SEQ ID NO: 4)

NH₂-DDKLP AEGLDIENS-COOH

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Preferred antibodies against IL1 α/β possess specific activity against at least one of the following peptide sequences:

NH₂-NCYSENEEDSSSID-COOH

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Preferred antibodies against IL6 possess specific activity against at least one of the following peptide sequences:

NH₂-APHRQPLTSSERIDKQI-COOH

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NH₂-QNRFESEEQARA-COOH

(SEQ ID NO: 13)

NH₂-AITPDPTTNAS-COOH

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Preferred antibodies against IL10 possess specific activity against at least one of the following peptide sequences:

NH₂-SPGQGTQSENSCT-COOH

(SEQ ID NO: 15)

NH₂-QMKDQLDNLLKES-COOH

(SEQ ID NO: 16)

NH₂-MPQAENQDPDIKA-COOH

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NH₂-LPCENKSKAVEQ-COOH

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NH₂-VRSSSRTPSDKPVA-COOH

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NH₂-KSPCQRETPEGAEAKPW-COOH

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These peptides are covalently bound to a carrier (KLH) according to a standard recipe. The conjugate dissolved in PBS is mixed in equal shares with Freund's adjuvant. The individual inoculation dose is set in such a way that it contains 200pg of the peptide belonging to the antigen in question. 15-week-old young hens are im-